UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,110	02/15/2001	Maurizio Zanetti	UCSD-07017	2849

7590 10/03/2006

MAHA A. HAMDAN
MEDLEN & CARROLL , LLP
101 HOWARD STREET, SUITE 350
SAN FRANCISCO ,, CA 94105

EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/788,110	ZANETTI, MAURIZIO	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *16 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *19,21,22 and 24-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *19,21,22 and 24-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/16/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 16, 2006 is acknowledged and has been entered. Claims 1-18 have been canceled, claims 19, 26 have been amended and new claims 36-41 have been added. An action on the RCE follows.

2 Claims 19, 21, 22, 24-41 are pending and currently under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds of Rejection

Claim Rejections - 35 USC 112

4. Claims 19, 21, 22, 24-41 are rejected under 35 USC 112, first paragraph because the specification, while enabling for a composition for the *in vitro* induction of cytotoxic T lymphocytes that lyse cancer cells, *in vitro,* upon recognition of naturally processed human telomerase transcriptase peptides comprising at least one of a polypeptide consisting of nine amino acids wherein said peptides are SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO: 16, SEQ ID NO:22 does not reasonably provide enablement for a composition for induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed human telomerase reverse transcription peptides comprising at least one HLA-A2.1 restricted TRT peptide nine amino acids in length of a human TRT protein consisting of a sequence set forth in SEQ ID NO:23. The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make/use the invention commensurate in scope with these claims.

The claims are drawn to a composition for induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed human telomerase reverse transcription peptides comprising at least one HLA-A2.1 restricted TRT peptide nine amino acids in length of a human TRT protein consisting of a sequence set forth in SEQ ID NO:23. This means that (1) the claims as broadly written are drawn to a composition for the induction of cytotoxic T lymphocytes that lyse cancer cells *in vivo*, that is a pharmaceutical composition for the treatment of cancer, (2) the claims as written are drawn to any nonomer of SEQ ID NO:23.

As previously set forth, the specification teaches that a method for treating tumors currently being evaluated makes use of telomerase, which normal body cells, other than sperm and the hematopoietic system, neither produce nor require. Attempts to develop a drug that will block the action of the enzyme sufficiently to either inhibit the growth of new tumor cells or cause the death of older ones have been made (page 5, lines 4-1). Despite the wide-ranging and expensive efforts expended in researching, developing and evaluating new treatments and cures for tumors and cancers, no truly significant advances or completely satisfactory treatments have thus far been achieved (p. 6, lines 15- 18). Applicant demonstrates that the majority of normal individuals and patients with prostate cancer express precursor telomerase reverse transcriptase (TRT) cytotoxic T lymphocytes (CTL) and when these are immunized *in vitro* against two HLA-A2.1 restricted peptides from hTRT, SEQ ID NOS 1 and 2, they develop hTRT specific CTL. This suggests the existence of precursor CTL for hTRT in the repertoire of normal individuals

and cancer patients. Most importantly, cancer patients CTL specifically lysed a variety of HLA-A2 cancer cell lines, demonstrating immunological recognition of endogenously-processed hTRT peptides. In addition, *in vivo* immunization of HLA-A2.1 transgenic mice generated a specific CTL response against both hTRT peptides. Thus, based on the induction of CTL responses *in vitro* and *in vivo* and the susceptibility to lysis of tumor cells of various origins by hTRT CTL, Applicant suggests that hTRT could serve as a universal cancer vaccine for humans (para bridging pages 10-1 1). The specification further teaches that it is reasonable that expression of hTRT in cancer cells is a likely source of peptides that, upon association with MHC Class 1 molecules, could target CTL to cancer cells and since high hTRT activity is widespread among human tumors, hTRT could serve as a universal tumor antigen for immunotherapy and vaccine approaches (para bridging pages 11-1 2). HTRT is encoded in the genome and is in all respects a self-antigen. Consequently, CD8+ T lymphocytes with a receptor for MHCl hTRT peptide complexes are expected to be eliminated during thymic negative selection, reducing the potential precursor T cell repertoire and imposing limitations on their expansion upon encounter with tumor cells in adult life. Additionally, stimulation by antigen in the absence of a second signal induces clonal anergy, further hampering the potential repertoire. The extent to which these events affect the normal adult repertoire and whether or not exposure to hTRT during cancer formation has any adverse effect on the ability of cancer patients to respond, is not known. Because answering these questions is relevant to future strategies of immune intervention targeted at hTRT, the ability of normal individuals and cancer patients to mount a CTL response *in vitro* against two hTRT peptides restricted by the HLA-A2 allele was analyzed (p. 12, lines 6-17).

The specification exemplifies *in vitro* immunization which leads to the production of hTRT specific CTT, and the *in vivo* production of CTL against hTRT peptides in an animal model that does not have a tumor burden. The specification further teaches that some hTRT peptides can expand precursor CTL in PBMC of both normal individuals and patients with prostate cancer and induce MHC Class I-restricted HLA-A2 restricted, peptide-specific CTL responses (para bridging pages 27-28). The specification further teaches that not all selected peptides were effective at generating *in vitro* killing of cancer cells (p. 27). In addition the specification further teaches that the available CTL repertoire for hTRT is preserved in normal individuals and in individuals with cancer which suggests that exposure to cancer does not cause deletion or anergy of clonotypes specific for hTRT (p. 28, lines 29-32).

The specification states that the PMBC of three therapy resistant patients with metastases responded to *in vitro* immunization with the exemplified peptides by developing hTRT CTL. It was surprising that the CTL could be induced at such an advanced stage of disease which is generally characterized by immunosuppression and given the above, it is expected that the two peptides identified in this study may be used for vaccinations for HLA-A2t cancer patients(para bridging pages 28-29).

As drawn to issue (1) lack of enablement for the broadly claimed method which reads a composition for the induction of cytotoxic T lymphocytes that lyse cancer cells *in vivo*, that is a pharmaceutical composition for the treatment of cancer, one cannot extrapolate the teaching of the specification to the scope of the claims because neither the *in vitro* nor the *in vivo* studies presented in the specification are commensurate in scope with the claimed invention. Applicant is

correct in the statement that despite the wide-ranging and expensive efforts expended in researching developing and evaluating new treatments and cures for tumors and cancers, no significant advances or completely satisfactory treatments have thus far been achieved.

Although applicant demonstrates *in vitro* expansion of CTL and *in vivo* production of CTL in a mouse model, the specification provides no nexus between these experiments and the broadly claimed composition that reads on the induction of cytotoxic T lymphocytes that lyse cancer cells *in vivo*, that is a pharmaceutical composition for the treatment of cancer, which is clearly contemplated in the specification for use in humans. In particular as drawn to the *in vitro* expansion exemplified, this exemplification is now enabling because the *in vitro* expansion system does not provide an intact immune system, the peptides that are used to induce CTL are in contact with the lymphocytes for long periods of time and the target cells are incubated with the CTL for long periods of time, neither of which occur in the *in vivo* environment. As drawn to the *in vivo* experiments disclosed, these experiments do not enable the claimed invention because the model does not include animals with tumor load. Although applicant states that it is reasonable that expression of hTRT in cancer cells is a likely source of peptides that, upon association with MHC Class 1 molecules, could target CTL to cancer cells and since high hTRT activity is widespread among human tumors, hTRT could serve as a universal tumor antigen for immunotherapy and vaccine approaches, the specification also states that CD8+ T lymphocytes with a receptor for MHC/hTRT peptide complexes are expected to be eliminated during thymic negative selection, reducing the potential precursor T cell repertoire and imposing limitations on their expansion upon encounter with tumor cells in adult life. Additionally, stimulatory

antigen in the absence of a second signal induces clonal anergy, further hampering the potential repertoire. In addition, although the specification clearly teaches that patients with advanced cancer produce CTL that lyse cancer cell lines *in vitro,* suggesting that the peptides processed are naturally processed peptides, it is clear that these CTL are not effective to effectively lyse the cancer cells in the patients given the advanced stage of their cancer and it would appear that it is more likely than not that (for the reasons of record and set forth below) that induction of CTL in patients that are reactive with the exemplified peptides would not be effective to lyse cancer cells or be an effective active vaccine *in vivo*.

In agreement with the teachings of the specification, the unpredictability of the effectiveness of compositions that stimulate CTL that lyse cancer cells are well known in the art. For example, Kirkin et al, of record teach that in particular for tumor antigens (even with the existence of precursor CTL), due to the existence of self-tolerance, only T cells with low affinity T-cell receptors are produced (abstract). Further, Chaux et al, of record teach some of the CTLs have an affinity that is too low for the recognition of cells that have processed the antigen, which is different from the *in vitro* conditions like those presented in the instant specification, in which the synthetic peptides are in high number when incubated with the cells (p.541, second column, second paragraph). Given the above, even if a peptide was recognized by T-cells *in vitro* from patients with cancer, it could not be predicted that the T-cells would recognize these peptides *in vivo* and if not recognized *in vivo*, it is clear that one would not know how to use the claimed peptides in a composition to produce T-cells to lyse cancer cells *in vivo*. Similarly Sherman et al, of record teach that self-tolerance may eliminate T cells that are capable of recognizing T-cell epitopes with high avidity , Smith, of record, teaches

that antigen overload, due to antigen shedding by actively growing tumor, could block specifically either cytotoxic or proliferative responses of tumor specific T cells (again, even if precursor CTL exist in the system) (p. 847, last paragraph bridging p.848 and p.848). Smith further teaches that many tumors progressively lose MHC representation at the surface of the cell, and the loss of surface Class I MHC could severely limit the possibilities for cytotoxic T cells specific for a tumor specific antigen to find said tumor specific antigen in the necessary MHC context (p.484). Given the above, one would not know how to use the broadly claimed composition.

In addition, Boon, of record teaches that for active immunization in human patients we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have occurred and it may prevent immunization and several lines of evidence, as set forth above, suggest that large tumor burdens can tolerize or at least depress the capability to respond against the tumor (p. 206, para 2). In addition, Boon teaches even if activated CTLs are significantly increased, the therapeutic success remains unpredictable due to inconsistencies in antigen expression or presentation by tumor cells (p. 178, paragraph before last paragraph). Thus based on the teaching in the art and in the specification, one cannot predict that an adequate *in vivo* T cell response useful for induction of cytotoxic T lymphocytes that lyse cancer cells, as contemplated and broadly claimed, could be induced by the peptides of the invention in patients having tumor burden as contemplated. In addition, again as drawn to the unpredictability of *in vivo* T-cell response induction, , Kirkin et al, *Supra* review several melanoma-associated antigens, including NY-ESOl, and conclude that initiation of a strong immune response *in vivo* is an extremely rare

event (p.674, first column, last paragraph). Kirkin et al teach that for some antigens, due to the existence of self-tolerance, only T cells with low affinity T-cell receptors are produced (abstract). Kirkin et a1 teach that although several peptides of melanoma associated antigens have been identified as recognized by CTL *in vitro,* and peptides from MAGE-A1 and MAGE-A3 have been tested for their ability to induce anti-melanoma immune response *in vivo,* only one of the peptides, peptide EVDPIGHLY of MAGE-A3, has limited anti-tumor activity, indicating their low immunogenicity p.666, second column, second paragraph, last 6 lines). Further, even this peptide EVDPIGHLY of MAGE-A3 produces a very low level of CTL response which is detectable only by a very sensitive method, as taught by Chaux et al, of record, abstract.

Finally, it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable. Although drawn to chemotherapeutic agents, the teachings of Gura (Science, 1997, 278:1041-1042) are relevant to the instant rejection. In particular, Gura teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs (which include immunotherapeutic protocols) have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for treatment of cancer (p. 1041, see first and second para). Given the above, because of the known unpredictability of the art, in the absence of experimental evidence in an appropriate animal model, with data commensurate in scope with the invention claimed, no one skilled in the art would believe it more likely than not that the claimed composition would function as broadly claimed based only upon the *in vitro* studies exemplified and the *in vivo* animal model

presented wherein the model did not include study of the effects of the broadly claimed composition on the lysis of cancer cells *in vivo*.

As drawn to issue (2), the use of any nonomer of SEQ ID NO:23 for the induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed human TRT peptides, the specification teaches, at paragraph 0044 of the published application that telomerase is a ribonucleoprotein enzyme which has been linked to malignant transformation in human cells. The generation of endogenously-processed telomerase peptides bound to Class I major histocompatibility complex (MHC) molecules could therefore target cytotoxic T lymphocytes (CTL) to tumors of different origins. This could advance vaccine therapy against cancer provided that precursor CTL recognizing telomerase peptides in normal adults and cancer patients can be expanded through immunization. Applicant demonstrates here that the majority of normal individuals and patients with prostate cancer immunized in vitro against two HLA-A2.1 restricted peptides from telomerase reverse transcriptase (hTRT), develop hTRT specific CTL. This suggests the existence of precursor CTL for hTRT in the repertoire of normal individuals and in cancer patients. Most importantly, cancer patients' CTL specifically lysed a variety of HLA-A2+ cancer cell lines, demonstrating immunological recognition of endogenously-processed hTRT peptides. Further the specification teaches that the studies disclosed in the specification show that 1) patients' CTL are specific for the hTRT peptide used to induce them, and 2) lysis of prostate cancer cells is mediated by, and is specific for, endogenously-processed hTRT peptides complexed with HLA-A2.1 molecules, suggesting chemical identity between naturally processed peptides on tumor cells and the synthetic peptides used for immunization. (para 0070 of the

published application). Finally, the specification teaches that not all selected peptides were effective at generating even *in vitro* killing of cancer cells (p. 27).

One cannot extrapolate the teaching of the specification to the scope of the claims because the specification as originally filed does not teach how to predictably distinguish between those peptides that will induce the CTL as claimed and those that do not. Although the specification identifies four peptides, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:16, SEQ ID NO:22 capable of inducing CTL that will lyse cancer cells *in vitro*, it is clear that the identification of these peptides was made by screening of the peptides to determine their activity as it is drawn to inducing CTL that recognize hTRT peptides. However, the screening assays taught and exemplified in the specification do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays are not sufficient to enable an invention since they are merely a wish or plan for obtaining the claimed chemical invention. It is clear that the specification does provide the necessary guidance to the practitioner to enable the making of the broadly claimed invention, that is the ability to predictably distinguish between those nonomers that will induce CTL that lyse cancer cells from those that will not.

The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the claimed invention would function as broadly claimed or as contemplated with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

Some of Applicant's arguments drawn to the prior rejection of claims 19, 21, 22, 24-35 under 35 USC 112, first paragraph are relevant to the instant rejection.

Applicant argues that the claimed invention is enabling for *in vitro* stimulation of CTL against cancer cells. The argument has been considered and has been found persuasive, in part and as set forth above, the claims-in-part, are enabled, by the specification, for the *in vitro* stimulation and induction of hTRT specific CTL that lyse cancer cells upon recognition of naturally processed hTRT peptides.

Applicant argues that MPEP 2164.01 teaches that when multiple uses for claimed compounds or compositions are disclosed in the application, the enablement rejection must include an explanation sufficiently supported by the evidence why the specification fails to enable each disclosed use. Applicant emphasis the teaching the "if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention". The argument has been considered but has not been found persuasive because Applicant is mischaracterizing the teachings of the MPEP. In point of fact, the MPEP specifically states that

> "**When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation** (emphasis added). See In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (claiming a chimeric gene capable of being expressed in any cyanobacterium and thus defining the claimed gene by its use). **In contrast, when a compound or composition claim is not limited by a recited use** (emphasis added), any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use. If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In

other words, **if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention.**" (emphasis added).

In the instant case, the claimed composition is limited by a particular use, that is "for the induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed hTRT peptides. The claims have been properly evaluated based on that limitation and the scope of claimed invention has properly been found to be unsupported by the specification as originally filed for the reasons set forth previously and above.

5. If Applicant were able to overcome the rejections set forth above, Claims 19, 21, 22, 24-41 would still be rejected under35 USC 112, first paragraph because the specification, while enabling for a composition that induces CTL upon recognition of hTRT peptides naturally processed by primary cancer cells, does not reasonably provide enablement for a composition for induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed human telomerase reverse transcription peptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The claims are drawn to a composition for induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed human telomerase reverse transcription peptides, this means induction of cytotoxic T lymphocytes that recognize naturally processed hTRT in cell lines that are not naturally processed in primary cancer cells.

As set forth above, the specification teaches induction of CTX that lyse both cell line and primary cancer cells upon recognition of hTRT peptides naturally processed by primary cancer cells, that is SEQ ID Nos 1 and 2 and further teaches

that a composition comprising SEQ ID NO:16 induced CTL that lysed melanoma cell line 624 (p. 27, lines 24-26) and that a modified hTRT peptide, SEQ ID NO:22 was shown to be suitable for inducing CTL that lysed human myeloma U266 cells (see tables at pages 27-28).

One cannot extrapolate the teaching of the specification to the scope of the claims because the specification provides no guidance as to whether any nonomer other than SEQ ID NOs 1 and 2 are capable of inducing CTX that lyse primary cancer cells upon recognition of TRT peptides naturally processed by said cancer cells. The specification provides no guidance drawn to which of the nonomers of SEQ ID NO;23, other than SEQ ID Nos 1 and 2 are naturally processed for presentation in primary cancer cells, no consensus sequence of such structure is taught in the specification or art of record. Applicant has clearly demonstrated that identification of peptides that are naturally processed by primary cancer cells requires assay of the primary cancer cell induced CTL to determine whether or not they are reactive with a particular peptide and other than a suggestion to screen, the specification provides no guidance on how to predictably distinguish between those nonomers that are naturally processed in primary cancer cells and those that are not. Again as set forth above, the screening assays taught and exemplified in the specification do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays are not sufficient to enable an invention since they are merely a wish or plan for obtaining the claimed chemical invention. It is clear that the specification does provide the necessary guidance to the practitioner to enable the making of the broadly claimed invention, that is the ability to predictably distinguish between those nonomers that will induce CTL that lyse primary cancer cells upon recognition of naturally

processed hTRT from those that will not. Given the above, one would not know how to predictably make the invention as broadly claimed, that is a composition that induces anti-hTRT CTL which lyse primary cancer cells. If one could not make a composition that induces ant-hTRT CTL against primary cancer cells, one would not how to use the claimed invention because the only apparent use of CTLs induced against hTRT that lyse, for example, cancer cell lines, but not primary cancer cells would be for the further characterization of cell lines, which is a use only for experimental purposes and not useful for real world purposes.

The specification provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the claimed invention would function as broadly claimed or as contemplated with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

6. Claims 19, 24-29, 33-35 are rejected under 35 USSC 112, first paragraph as lacking an adequate written description in the specification.

Claims 19, 24-29, 33-35 are drawn to a composition for induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed hTRT peptides wherein the composition comprises at least one HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, a modified peptide. Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v.

Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir.

2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).
The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

Thus, the instant specification may provide an adequate written description of a composition for induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed hTRT peptides wherein the composition comprises at least one HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, a modified peptide, per Lilly by structurally describing a representative number of HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, a modified peptide, that function as claimed or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the composition for induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of

naturally processed hTRT peptides wherein the composition comprises at least one HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, a modified peptide, in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, a modified peptide that induces lysis of lyse cancer cells upon recognition of naturally processed hTRT peptide, nor does the specification provide any partial structure of such HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, a modified peptide that induces lysis of lyse cancer cells upon recognition of naturally processed hTRT peptide, nor any physical or chemical characteristics of the HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, a modified peptide that induces lysis of lyse cancer cells upon recognition of naturally processed hTRT peptide, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification describes SEQ ID Nos 1, 2, 16, 22 these peptides do not provide a description of HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, a modified peptide that induces lysis of lyse cancer cells upon recognition of naturally processed hTRT peptide, that would satisfy the standard set out in Enzo because only SEQ ID Nos 1 and 2 have been disclosed to be naturally processed hTRT peptides and no common structure function relationship is disclosed that would identify SEQ ID Nos 16 and 22 as naturally processed hTRT.

The specification also fails to describe the HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23 by the test set out in Lilly. The specification describes only the two "naturally processed" peptides.

Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, a modified peptide, that is required to practice the claimed invention.

7. Claims 26-28, 33-35 are rejected under 35 USSC 112, first paragraph as lacking an adequate written description in the specification.

Claims 19, 24-29, 33-35 are drawn to a composition for induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed hTRT peptides wherein the composition comprises at least one HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23 wherein said TRT peptide comprises a modification to enhance binding to HLA-A2.1. Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between

function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).
The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

Thus, the instant specification may provide an adequate written description of a composition for induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed hTRT peptides wherein the composition comprises at least one HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, wherein said TRT peptide comprises a modification to enhance binding to HLA-A2.1, per Lilly by structurally describing a representative number of HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23 wherein said TRT peptide comprises a modification to enhance binding to HLA-A2.1, that function as claimed or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the composition for induction of cytotoxic T lymphocytes that lyse cancer cells upon recognition of naturally processed hTRT peptides wherein the composition comprises at least one HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23 wherein said TRT peptide comprises a modification to enhance binding to HLA-A2.1, in a manner that satisfies either the Lilly or Enzo standards. The

specification does not provide the complete structure of any HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, a modified peptide that induces lysis of lyse cancer cells upon recognition of naturally processed hTRT peptide wherein said TRT peptide comprises a modification to enhance binding to HLA-A2.1, nor does the specification provide any partial structure of such HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, wherein said TRT peptide comprises a modification to enhance binding to HLA-A2.1 that induces lysis of cancer cells upon recognition of naturally processed hTRT peptide, nor any physical or chemical characteristics of the HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, wherein said TRT peptide comprises a modification to enhance binding to HLA-A2.1 that induces lysis of cancer cells upon recognition of naturally processed hTRT peptide, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification describes a single tyrosine substitution at position 1 of a canonical HLA-A2.1 motif that functions to enhance induction, this does not provide a description of HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, wherein said TRT peptide comprises a modification to enhance binding to HLA-A2.1 that induces lysis of cancer cells upon recognition of naturally processed hTRT peptide, that would satisfy the standard set out in Enzo.

The specification also fails to describe the HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23 wherein said TRT peptide comprises a modification to enhance binding to HLA-A2.1 by the test set out in Lilly. The specification describes only a single modification, that is the

tyrosine substitution at position 1 of a canonical HLA-A2.1 motif. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the HLA-A2.1-restricted hTRT peptide nine amino acid residues in length from SEQ ID NO:23, wherein said TRT peptide comprises a modification to enhance binding to HLA-A2.1 that is required to practice the claimed invention.

8. Claims 19, 21, 22, 24-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19, 21, 22, 24-41 are indefinite in the recitation of the phrase "naturally processed hTRT peptides". The phrase is indefinite because the only teaching in the specification drawn to "naturally processed" is found in paragraph 0077 of the published application wherein the specification teaches that " experiments were performed in an attempt to understand if lysis of the LnCap tumor cell line was specific for endogenously-processed hTRT peptides. In these experiments the lysis of LnCap cells by CTL from a prostate cancer patient was competed for by T2 cells pulsed *in vitro* with p540 or p865 (10 .mu.g/ml). Peptide-loaded T2 cells caused a dose-dependent inhibition of lysis of LnCap cells in both peptide combinations ..... these studies show that 1) patients' CTL are specific for the hTRT peptide used to induce them, and 2) lysis of prostate cancer cells is mediated by, and is specific for, endogenously-processed hTRT peptides complexed with HLA-A2.1 molecules, suggesting chemical identity between

naturally processed peptides on tumor cells and the synthetic peptides used for immunization." Thus it appears that the phrase "naturally processed" is drawn to peptides processed on primary cancer cells. However, no definition for "naturally processed" is found in the specification, therefore the metes and bounds of patent protection claimed cannot be determined because naturally processed could be interpreted as either naturally processed in vivo or naturally processed in any cell line *in vitro*, regardless of whether or not this natural processing *in vivo*, thus the metes and bounds of patent protection claimed cannot be determined.

9. All other objections and rejections previously set forth are hereby withdrawn.

10. No claims allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
August 29, 2006